

**Remarks**

Prior to the amendments herein, claims 1-3, 5-10, 12-14, 16-21, 23, 25-27, 29-34, 36, 37, and 39-52 were pending. Claims 1, 12, 23, 25, 27, 29, 31-34, 36-37 are amended herein for clarity. Claims 5-9 and 16-20 are amended herein to correct a recurring typographical error, *i.e.*, the omission in each claim of a hyphen between “insulin” and “producing.” Claims 2, 3, 13, 14, 26, 30 and 39-52 are canceled herein without prejudice. New claims 53-74 are added herein. Support for these amendments and new claims can be found in the original claim language and throughout the specification, as set forth below. It is believed that these amendments and new claims add no new matter. In light of these amendments, new claims, and the following remarks, applicants respectfully request reconsideration of this application, entry of these amendments and new claims, and allowance of the claims to issue.

Applicants acknowledge withdrawal of numerous previous objections and rejections. Applicants also express their appreciation for Examiner Jiang’s and Examiner Kemmerer’s participation in a telephonic interview with the undersigned on March 21, 2005.

**35 U.S.C. § 112, second paragraph**

Claims 1-3, 5-10, 12-14, 16-21, 23, 25-27, 29-34, 36, 37 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Office Action states that claim 1 is indefinite for the recitation of “and a fragment of the preceding GLP-1 peptides.”

Claims 2, 3, 13, 14, 26 and 30 are canceled herein without prejudice, thereby rendering moot these rejections as applied to these claims. Therefore, applicants respectfully request withdrawal of these rejections.

Claims 1, 12, 23, 27, 32-34 and 36 are amended herein according to the Examiner’s suggestion by adding the term “any one of” before “the preceding.” Claim 31 is amended herein

**ATTORNEY DOCKET NO. 14014.0346U1**  
**Application No. 09/762,538**

by adding the word “one” before “of the preceding.” Applicants believe that these amendments overcome the rejections of claims 1, 5-10, 12, 16-21, 23, 25, 27, 29, 31-34, 36 and 37 and respectfully request withdrawal of these rejections.

The Office Action states that claims 3 and 14 are indefinite for the recitation “with the substance *in vivo*.” Claims 3 and 14 are canceled herein without prejudice, rendering these rejections moot. Thus, applicants respectfully request withdrawal of these rejections.

35 U.S.C. § 102

A. Claims 23, 26, 27, 30, 31, 36 and 37 remain rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Eng (U.S. Patent No. 5,424,286, the ‘286 patent). Specifically, the Office Action states that the present claims “do not distinguish themselves from the prior art in the active ingredient used and *method steps*” (emphasis present, Office Action pages 3-4). The Office Action goes on to state that because the active ingredient and the method steps used are the same between the prior art and the present invention, the results or the consequences would be inherently the same.

Claims 26 and 30 are canceled herein without prejudice, rendering moot these rejections as applied to these claims. Therefore, applicants respectfully request withdrawal of these rejections. The following arguments, thus, address the rejections of claims 23, 27, 31, 36 and 37.

For a prior art reference to anticipate a claimed invention, each and every element of the claimed invention must be disclosed in that single reference. Further, the disclosure in that single reference must be enabling. If one element of the claimed invention is not disclosed in the prior art reference, there is no anticipation. It is settled law that “[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently.” *Verdegaal v. Union Oil*, 814 F.2d 628, 2 U.S.P.Q.2d 1051 (Fed. Cir. 1987).

Claim 23 is amended herein to include a method step, “administering by one or more injections of a substance to the subject daily for at least three days an amount of the substance effective to induce differentiation of non-insulin-producing cells into insulin-producing cells.”

Support for this amendment can be found in the specification on page 42, lines 4-12 and page 20, lines 1-28. This method step distinguishes the claimed invention from the '286 patent.

The '286 patent does not disclose each and every element of amended claim 23. Specifically, in the '286 patent, one does not find the method of differentiating non-insulin-producing cells into insulin-producing cells in a subject in need thereof, comprising administering by one or more injections of a substance to the subject daily for at least three days an amount of the substance effective to induce differentiation of non-insulin-producing cells into insulin-producing cells, wherein the substance is selected from the group consisting of a GLP-1 peptide, a GLP-1 peptide containing one or more conservative amino acid substitutions at positions other than positions 7, 10, 12, 13 and 15 of GLP-1, and a fragment of any one of the preceding GLP-1 peptides, and wherein the GLP-1 peptide or fragment thereof has the ability to differentiate non-insulin-producing cells into insulin-producing cells. In fact, none of the experiments in the cited art lasted longer than four hours. See Example 2, col. 6, line 22 to col. 7, line 31 and Figure 3 in the '286 patent.

Thus, because the '286 patent does not contain each and every element of the claimed invention, there is no anticipation. Therefore, applicants respectfully request withdrawal of this rejection.

Claim 27 is amended herein to include the method step, "administering by one or more injections of a substance to the subject daily for at least two days an amount of the substance effective to induce differentiation of non-insulin-producing cells into insulin-producing cells." Support can be found in the specification on page 42, lines 4-12 and page 20, lines 1-28. This method step distinguishes the claimed invention from the '286 patent.

The '286 patent does not disclose each and every element of amended claim 27. Specifically, in the '286 patent, one does not find the method of differentiating non-insulin-producing cells into insulin-producing cells in a subject in need thereof, comprising administering by one or more injections of a substance to the subject daily for at least two days

an amount of the substance effective to induce differentiation of non-insulin-producing cells into insulin-producing cells wherein the substance is selected from the group consisting of an Exendin-4 peptide, an Exendin-4 peptide containing one or more conservative amino acid substitutions at positions other than positions 1, 4, 6, 7 and 9 of Exendin-4, and a fragment of any one of the preceding Exendin-4 peptides, and wherein the Exendin-4 peptide or fragment thereof has the ability to differentiate non-insulin-producing cells into insulin-producing cells. In fact, none of the experiments in the cited art lasted longer than four hours. See Example 2, col. 6, line 22 to col. 7, line 31 and Figure 3 in the '286 patent.

Thus, because the '286 patent does not provide each and every element of the claimed invention, there is no anticipation. Therefore, applicants respectfully request withdrawal of this rejection.

Claim 31 is amended herein by adding the term "an isolated" before "population of cells" and by adding the term "*in vitro*." Support can be found in the original claim language and in the specification on page 42, lines 14-16. The addition of these limitations distinguishes the claimed invention from the '286 patent.

The '286 patent does not disclose each and every element of amended claim 31; thus, there is no anticipation. Therefore, applicants respectfully request withdrawal of this rejection.

Claim 36 is amended herein to include the method step, "administering by one or more injections of a substance to the subject daily for at least two days." Support can be found in the specification on page 42, lines 4-12 and page 20, lines 1-28. This method step distinguishes the claimed invention from the '286 patent.

The '286 patent does not disclose each and every element of amended claim 36. Specifically, in the '286 patent, one does not find the method of inducing insulin secretion in a subject in need thereof and lacking insulin-producing cells, comprising administering by one or more injections of a substance to the subject daily for at least two days an amount of the substance effective to induce insulin production, wherein the substance is selected from the

**ATTORNEY DOCKET NO. 14014.0346U1**  
**Application No. 09/762,538**

group consisting of an Exendin-4 peptide, an Exendin-4 peptide containing one or more conservative amino acid substitutions at positions other than 1, 4, 6, 7 and 9 of Exendin-4, and a fragment of any one of the preceding Exendin-4 peptides, and wherein the Exendin-4 peptide or fragment thereof has the ability to differentiate non-insulin-producing cells into insulin-producing cells. In fact, none of the experiments in the cited art lasted more than four hours. See Example 2, col. 6, line 22 to col. 7, line 31 and Figure 3 in the '286 patent.

Thus, because the '286 patent does not provide each and every element of the claimed invention, there is no anticipation. Therefore, applicants respectfully request withdrawal of this rejection and withdrawal of the rejection of dependent claim 37.

B. Claims 23, 26 and 31 remain rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Dupre (WO 95/31214) for the reasons set forth in previous Office Actions and for the reasons alleged above.

Claim 26 is canceled herein without prejudice, thereby rendering moot this rejection as it applies to this claim. Therefore, applicants respectfully request withdrawal of this rejection.

Claim 23 is amended herein to include the method step, "administering by one or more injections of a substance to the subject daily for at least three days an amount of the substance effective to induce differentiation of non-insulin-producing cells into insulin-producing cells." Support can be found in the specification on page 42, lines 4-12 and page 20, lines 1-28. This method step distinguishes the claimed invention from Dupre.

Dupre does not disclose each and every element of amended claim 23. Specifically, in Dupre, one does not find the method of differentiating non-insulin-producing cells into insulin-producing cells in a subject in need thereof, comprising administering by one or more injections of a substance to the subject daily for at least three days an amount of the substance effective to induce differentiation of non-insulin-producing cells into insulin-producing cells, wherein the substance is selected from the group consisting of a GLP-1 peptide, a GLP-1 peptide containing one or more conservative amino acid substitutions at positions other than positions 7, 10, 12, 13

and 15 of GLP-1, and a fragment of any one of the preceding GLP-1 peptides, and wherein the GLP-1 peptide or fragment thereof has the ability to differentiate non-insulin-producing cells into insulin-producing cells. In fact, in Dupre, GLP-1 was administered to test subjects either only once subcutaneously (see Examples 4-6, page 10, line 19 through page 11, line 12) or by continuous infusion that lasted for no more than 2 hours (see Examples 1-3, page 9, line 12 through page 10, line 16).

Thus, because Dupre does not provide each and every element of the claimed invention, there is no anticipation. Therefore, applicants respectfully request withdrawal of this rejection.

Claim 31 is amended herein by adding the term “an isolated” before “population of cells” and by adding the term “*in vitro*.” Support can be found in the original claim language and in the specification on page 42, lines 14-16. The addition of these limitations distinguishes the claimed invention from Dupre.

Dupre does not disclose each and every element of amended claim 31. Specifically, in Dupre, one does not find the method of enriching an isolated population of cells for insulin-producing cells, comprising contacting non-insulin-producing cells *in vitro* for at least twenty-four hours. In fact, Dupre discloses administering GLP-1 to subjects and does not teach any *in vitro* methods.

Thus, because Dupre does not provide each and every element of the claimed invention, there is no anticipation. Therefore, applicants respectfully request withdrawal of this rejection.

C. Claims 23, 26 and 31 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Edvell *et al.* (*Experimental and Clinical Endocrinology & Diabetes*, 1997, 105(4)). Specifically, the Office Action states that Edvell *et al.* discloses a method for testing the effect of GLP-1 on food intake and insulin release by injecting GLP-1 twice daily for two days and therefore anticipates the claimed invention.

**ATTORNEY DOCKET NO. 14014.0346U1**  
**Application No. 09/762,538**

Claim 26 is canceled herein without prejudice, thereby rendering moot this rejection as it applies to this claim. Therefore, applicants respectfully request withdrawal of this rejection.

Claim 23 is amended herein to include the method step, “administering by one or more injections of a substance to the subject daily for at least three days an amount of the substance effective to induce differentiation of non-insulin-producing cells into insulin-producing cells.” Support can be found in the specification on page 42, lines 4-12 and page 20, lines 1-28. This method step distinguishes the claimed invention from Edvell *et al.*

Edvell *et al.* does not disclose each and every element of amended claim 23. Specifically, in Edvell *et al.*, one does not find the method of differentiating non-insulin-producing cells into insulin-producing cells in a subject in need thereof, comprising administering by one or more injections of a substance to the subject daily for at least three days an amount of the substance effective to induce differentiation of non-insulin-producing cells into insulin-producing cells, wherein the substance is selected from the group consisting of a GLP-1 peptide, a GLP-1 peptide containing one or more conservative amino acid substitutions at positions other than positions 7, 10, 12, 13 and 15 of GLP-1, and a fragment of any one of the preceding GLP-1 peptides, and wherein the GLP-1 peptide or fragment thereof has the ability to differentiate non-insulin-producing cells into insulin-producing cells. In fact, in Edvell *et al.*, GLP-1 was administered to lean mice by twice daily injections for only two days, not at least three days.

Thus, because Edvell *et al.* does not contain each and every element of the claimed invention, there is no anticipation. Therefore, applicants respectfully request withdrawal of this rejection.

Claim 31 is amended herein by adding the term “an isolated” before “population of cells” and by adding the term “*in vitro*.” Support can be found in the original claim language and in the specification on page 42, lines 14-16. The addition of these limitations distinguishes the claimed invention from Edvell *et al.*

**ATTORNEY DOCKET NO. 14014.0346U1**  
**Application No. 09/762,538**

Edvell *et al.* does not disclose each and every element of amended claim 31. Specifically, in Edvell *et al.*, one does not find the method of enriching an isolated population of cells for insulin-producing cells, comprising contacting non-insulin-producing cells *in vitro* for at least twenty-four hours. In fact, Edvell *et al.* discloses administering GLP-1 to 20 days-old lean mice by twice daily injections for two days and does not teach any *in vitro* methods.

Thus, because Edvell *et al.* does not contain each and every element of the claimed invention, there is no anticipation. Therefore, applicants respectfully request withdrawal of this rejection.

New claims

New claims 53-74 are added herein. For the reasons stated above, applicants believe that the prior art does not disclose or suggest the claimed invention. Therefore, new claims 53-74 are patentable.

Pursuant to the above amendments and remarks, reconsideration and allowance of the pending application are believed to be warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

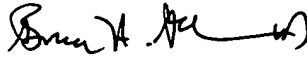
A Credit Card Payment Form PTO-2038 authorizing payment in the amount of \$1,220.00 (\$1,020.00 fee for a three (3) month extension of time and \$200.00 fee for new claims) and a Request for Extension of Time are enclosed. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.



**ATTORNEY DOCKET NO. 14014.0346U1**  
**Application No. 09/762,538**

Respectfully submitted,

NEEDLE & ROSENBERG, P.C.

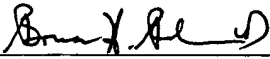


Bruce H. Becker, M.D., J.D.  
Registration No. 48,884

NEEDLE & ROSENBERG, P.C.  
Customer Number 36339  
(678) 420-9300  
(678) 420-9301 (fax)

**CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8**

I hereby certify that this correspondence, including any items indicated as attached or included, is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date indicated below.



Bruce H. Becker, M.D., J.D.

3/25/05

Date